

What is claimed is:

1. A nucleic acid ligand to hepatocyte growth factor/scatter factor (HGF) identified according to the method comprising:

a) preparing a candidate mixture of nucleic acids;

b) contacting the candidate mixture of nucleic acids with HGF, wherein nucleic acids having an increased affinity to HGF relative to the candidate mixture may be partitioned from the remainder of the candidate mixture;

c) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture;

d) amplifying the increased affinity nucleic acids to yield a mixture of nucleic acids enriched for nucleic acids with relatively higher affinity and specificity for binding to HGF, whereby a nucleic acid ligand of HGF may be identified.

2. A purified and isolated non-naturally occurring nucleic acid ligand to HGF.

3. A purified and non-naturally occurring RNA ligand to HGF wherein said ligand is selected from the group consisting of SEQ ID NOS:12-14 in FIGURE 7, SEQ ID NOS:15-17 in FIGURE 8, SEQ ID NOS:18-93 in Table 2, SEQ ID NOS:94-131 in Table 3, SEQ ID NOS:132-155 in Table 5, and SEQ ID NOS:156-159 in Table 7.

4. The nucleic acid ligand of claim 1 wherein HGF is associated with a solid support, and wherein steps b)-c) take place on the surface of said solid support.

5. The nucleic acid ligand of claim 4 wherein said solid support is comprised of nitrocellulose.

6. The nucleic acid ligand of claim 1 wherein said candidate mixture of nucleic acids is comprised of single stranded nucleic acids.

7. The nucleic acid ligand of claim 6 wherein said single stranded nucleic acids are ribonucleic acids.

8. The nucleic acid ligand of claim 6 wherein said single stranded nucleic acids are deoxyribonucleic acids.

9. The nucleic acid ligand of claim 7 wherein said candidate mixture of nucleic acids comprises 2'-F (2'-fluoro) modified ribonucleic acids.

10. The purified and isolated non-naturally occurring nucleic acid ligand of claim 2 wherein said nucleic acid ligand is single stranded.

11. The purified and isolated non-naturally occurring nucleic acid ligand of claim 10 wherein said nucleic acid ligand is RNA.

12. The purified and isolated non-naturally occurring RNA ligand of claim 11 wherein said ligand is comprised of 2'-fluoro (2'-F) modified nucleotides.

13. A method for the treatment of a tumor comprising administering a biologically effective dose of a nucleic acid ligand to HGF.

14. A method for determining the level of HGF in an individual comprising:

providing a nucleic acid ligand to HGF;

contacting a biological fluid from said individual with said nucleic acid ligand;

determining the amount of HGF that has bound to said nucleic acid ligand.

15. A method for inhibiting angiogenesis, the method comprising administering a biologically-effective dose of a nucleic acid ligand to HGF.

16. A pharmaceutical composition for the treatment of a tumor comprising a nucleic acid ligand to HGF and a pharmaceutically acceptable excipient.

17. A nucleic acid ligand to c-met identified according to the method comprising:

a) preparing a candidate mixture of nucleic acids;

b) contacting the candidate mixture of nucleic acids with c-met, wherein nucleic acids having an increased affinity to c-met relative to the candidate mixture may be partitioned from the remainder of the candidate mixture;

c) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture;

d) amplifying the increased affinity nucleic acids to yield a mixture of nucleic acids enriched for nucleic acids with relatively higher affinity and specificity for binding to c-met, whereby a nucleic acid ligand of c-met may be identified.

18. A purified and isolated non-naturally occurring nucleic acid ligand to c-met.

19. A purified and non-naturally occurring RNA ligand to HGF wherein said ligand is selected from the group consisting of SEQ ID NOS:160-174 in Table 9 and SEQ ID NOS:175-185 in Table 10.

20. The nucleic acid ligand of claim 17 wherein c-met is associated with a solid support, and wherein steps b)-c) take place on the surface of said solid support.

21. The nucleic acid ligand of claim 20 wherein said solid support is comprised of nitrocellulose.

22. The nucleic acid ligand of claim 17 wherein said candidate mixture of nucleic acids is comprised of single stranded nucleic acids.

23. The nucleic acid ligand of claim 22 wherein said single stranded nucleic acids are ribonucleic acids.

24. The nucleic acid ligand of claim 22 wherein said single stranded nucleic acids are deoxyribonucleic acids.

25. The nucleic acid ligand of claim 23 wherein said candidate mixture of nucleic acids comprises 2'-F (2'-fluoro) modified ribonucleic acids.

26. The purified and isolated non-naturally occurring nucleic acid ligand of claim 18 wherein said nucleic acid ligand is single stranded.

27. The purified and isolated non-naturally occurring nucleic acid ligand of claim 26 wherein said nucleic acid ligand is RNA.

28. The purified and isolated non-naturally occurring RNA ligand of claim 27 wherein said ligand is comprised of 2'-fluoro (2'-F) modified nucleotides.

29. A method for the isolation of nucleic acid ligands to c-met, comprising:

a) preparing a candidate mixture of nucleic acids;

b) contacting the candidate mixture of nucleic acids with c-met, wherein nucleic acids having an increased affinity to c-met relative to the candidate mixture may be partitioned from the remainder of the candidate mixture;

c) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture;

d) amplifying the increased affinity nucleic acids to yield a mixture of nucleic acids enriched for nucleic acids with relatively higher affinity and specificity for binding to c-met, whereby a nucleic acid ligand of c-met may be identified.

30. The method of claim 29 wherein said candidate mixture comprises single-stranded nucleic acids.

31. The method of claim 30 wherein said single-stranded nucleic acids comprise ribonucleic acids.

32. A method for the treatment of a tumor comprising administering a biologically effective dose of a nucleic acid ligand to c-met.

5 33. A method for inhibiting angiogenesis, the method comprising administering a biologically-effective dose of a nucleic acid ligand to c-met.

34. A pharmaceutical composition for the treatment of a tumor comprising a nucleic acid ligand to c-met and a pharmaceutically acceptable excipient.

10 25. A method for treating a disease in which elevated HGF is a causative factor, the method comprising administering a biologically-effective dose of a nucleic acid ligand to HGF.

36. A method for inhibiting tumor development, the method comprising administering a biologically effective dose of a nucleic acid ligand to HGF in combination with a biologically effective dose of a nucleic acid ligand to vascular endothelial growth factor (VEGF).

15 37. A method for inhibiting tumor development, the method comprising administering a biologically effective dose of a nucleic acid ligand to HGF in combination with a biologically effective dose of a nucleic acid ligand to basic fibroblast growth factor (bFGF).

20 38. A method for inhibiting tumor development, the method comprising administering a biologically effective dose of a nucleic acid ligand to HGF in combination with a biologically effective dose of a nucleic acid ligand to vascular endothelial growth factor (VEGF) and a biologically effective dose of a nucleic acid ligand to basic fibroblast growth factor (bFGF).

39. A method for inhibiting tumor development, the method comprising administering biologically effective doses of nucleic acid ligands to at least two growth factors.

25 40. The method of claim 39 wherein said growth factors are selected from the group consisting of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF $\beta$ ), HGF, and keratinocyte growth factor (KGF).

41. A method for inhibiting tumor development, the method comprising administering biologically effective doses of nucleic acid ligands to at least two receptors of growth factors.

30 42. The method of claim 41 wherein said growth factors are selected from the group consisting of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF $\beta$ ), HGF, and keratinocyte growth factor (KGF).

43. A method of inhibiting tumor development, the method comprising administering biologically-effective doses of nucleic acid ligands to one or more receptors of growth factors in combination with biologically-effective doses of nucleic acid ligands to one or more growth factors.

5        44. The method of claim 44 wherein said growth factors are selected from the group consisting of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF $\beta$ ), HGF, and keratinocyte growth factor (KGF).

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